GP1624

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February 25, 2004

CERTIFICATE OF MAILING
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February 25, 2004 — Date
Sharon A. Beresford

MS DD
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

RE: *U.S. Patent Application No. 10/665,377 entitled "OPIATE ANALOGS SELECTIVE FOR THE δ-OPIOID RECEPTOR" – William J. Welsh et al.*
Our reference: UVMO:021US
Client reference: 02UMS028

Sir:

Enclosed for filing in the above-referenced patent application is an Information Disclosure Statement, Form PTO-1449, and references A1-A6, B1, and C1-C40.

No fees are believed to be due in connection with the filing of this Information Disclosure Statement, however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be deemed necessary for any reason relating to the enclosed materials, the Commissioner is authorized to deduct the appropriate fees from Fulbright & Jaworski Deposit Account No.: 50-1212/UVMO:021US..

Please date stamp and return the enclosed postcard evidencing receipt of these materials.

Respectfully submitted,

Sharon A. Beresford
Reg. No. 52,615
Patent Agent

SAB/kmv
Encl.: as noted

25387000.1

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
William J. Welsh *et al.*

Serial No.: 10/665,377

Filed: September 18, 2003

For: OPIATE ANALOGS SELECTIVE FOR THE δ-OPIOID RECEPTOR

Group Art Unit: 1624

Examiner: Unknown

Atty. Dkt. No.: UVMO:021US

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Sharon A. Beresford

INFORMATION DISCLOSURE STATEMENT

MS DD
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

In compliance with the duty of disclosure under 37 C.F.R. § 1.56, it is respectfully requested that this Information Disclosure Statement be entered and the documents listed on attached Form PTO-1449 be considered by the Examiner and made of record. Copies of the listed documents required by 37 C.F.R. § 1.98(a)(2) are enclosed for the convenience of the Examiner.

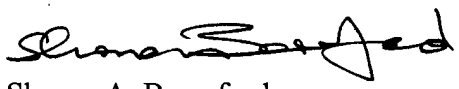
In accordance with 37 C.F.R §§ 1.97(g), (h), this Information Disclosure Statement is not to be construed as a representation that a search has been made, and is not to be construed to be

an admission that the information cited is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

The present Information Disclosure Statement is being filed prior to the receipt of a first Official Action reflecting an examination on the merits, and hence is believed to be timely filed in accordance with 37 C.F.R § 1.97(b). No fees are believed to be due in connection with the filing of this Information Disclosure Statement, however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be deemed necessary for any reason relating to these materials, the Commissioner is authorized to deduct the appropriate fees from Fulbright & Jaworski Deposit Account No.: 50-1212/UVMO:021US.

Applicants respectfully request that the listed documents be made of record in the present case.

Respectfully submitted,



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Agent for Applicants

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Date: February 25, 2004

Form PTO-1449 (modified)	Atty. Docket No. UVMO:021US	Serial No. 10/665,377
List of Patents and Publications for Applicant's	**Applicant** William J. Welsh *et al.*	
INFORMATION DISCLOSURE STATEMENT		
(Use several sheets if necessary)	**Filing Date:** September 18, 2003	**Group:** 1624

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U.S. Patent Documents	Foreign Patent Documents	Other Art
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U.S. Patent Documents

Exam. Init.	Ref. Des.	Document Number	Date	Name	Class	Sub Class	Filing Date of App.
	A1	5,436,249	07/25/95	Dappen *et al.*	514	279	05/16/94
	A2	5,922,887	07/13/99	Dondio and Ronzoni	548	539	05/20/96
	A3	6,359,111	05/19/02	Meyer and Kasina	530	302	05/27/99
	A4	5,298,622	03/29/94	Portoghese *et al.*	546	15	05/12/93
	A5	5,457,208	10/10/95	Portoghese and Olmsted	546	35	06/21/93
	A6	4,816,586	03/28/89	Portoghese	544	340	07/29/87

Foreign Patent Documents

Exam. Init.	Ref. Des.	Document Number	Date	Country	Class	Sub Class	Translation Yes/No
	B1	WO 99/67206	12/29/99	PCT			

Other Art (Including Author, Title, Date Pertinent Pages, Etc.)

Exam. Init.	Ref. Des.	Citation
	C1	Abdelhamid *et al.*, "Selective blockage of Delta opiod receptors prevents the development of morphine tolerance and dependence in mice," *J. Pharmacol. Exp. Ther.*, 258(1):299-303, 1991.
	C2	Akil *et al.*, "Endogenous opioids: biology and function," *Annual Rev. Neurosci.*, 7:223-255, 1984.
	C3	Ananthan *et al.*, "Synthesis, opioid receptor binding, and bioassay of naltrindole analogues substituted in the indolic benzene moiety," *J. Med. Chem.*, 41(15):2872-2881, 1998.
	C4	Ananthan *et al.*, "Synthesis, opioid receptor binding, and biological activities of naltrexone-derived pyrido- and pyrimidomorphinans," *J. Med. Chem.*, 42(18):3527-3538, 1999.
	C5	Bertolucci *et al.*, "Microdialysis of opioid peptide release from the nucleus accumbens and ventrical pallidum of the freely moving rat," *Neurosci. Abstr.*, 18L1368, 1992.
	C6	Blisky *et al.*, "SNC 80, a selective, nonpeptidic and systemically active opioid delta agonist," *J. Pharmacol. Exp. Ther.*, 273(1):359-366, 1995.

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U.S. Patent Documents	Foreign Patent Documents	Other Art
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Other Art (Including Author, Title, Date Pertinent Pages, Etc.)

Exam. Init.	Ref. Des.	Citation
	C7	Bradbury *et al.*, "Biosynthetic origin and receptor conformation of methionine enkephalin," *Nature*, 260:165-166, 1976.
	C8	Conn *et al.*, "An unusual fischer indole synthesis with 4-keto acids: an indole incorporating the terminal hydrazine nitrogen," *J. Org. Chem.*, 55(90):2908-2913, 1990.
	C9	Coombs *et al.*, "Intrathecal morphine tolerance: use of intrathecal clonidine, DADLE, and intraventricular morphine," *Anesthesiology*, 62(3):358-363, 1985.
	C10	Cramer III *et al.*, "Comparative molecular field analysis (CoMFA). 1. Effect of shape on binding of steroids to carrier proteins," *J. of the Am. Chem. Soc.*, 110(18):5959-5967, 1988.
	C11	Dressman and Lennernas, In: *Oral Drug Absorption: Prediction and Assessment (Drugs and the Pharmaceutical Sciences)*, Vol. 106, 2000.
	C12	Foley, In: *Handbook of Experimental Pharmacology*, Herz (ed.), Vol. 104/II: Opioids II, Springer-Verlag, Berlin, 693-743, 1993.
	C13	Gomes-Flores and Weber, "Differential effects of buprenorphine and morphine on immune and neuroendocrine functions following acute administration in the rat mesencephalon periaqueductal gray," *Immunopharm.*, 48:145-156, 2000.
	C14	Hardman and Limbird, In: *Goodman & Gilman's The Pharmacological Basis of Therapeutics*, 10th ed., McGraw-Hill Professional Publishing, 2001.
	C15	House *et al.*, "Suppression of immune function by non-peptidic delta opioid receptor antagonists," *Neurosci. Lett.*, 198:119, 1995.
	C16	Hughes *et al.*, "Identification of two related pentapeptides from the brain with potent opiate agonist activity," *Nature*, 258:577-579, 1975.
	C17	Kaliszan *et al.*, "Gradient HPLC in the determination of drug lipophilicity and acidity," *Pure Appl. Chem.*, 73:1465-1475, 2001.
	C18	Knapp *et al.*, "Properties of TAN-67, a nonpeptidic δ-opioid receptor agonist, at cloned human δ- and μ-opioid receptors," *Eur. J. Pharmacol.*, 291(2):129-134, 1995.
	C19	Knapp *et al.*, "Structure-activity relationships for SNC80 and related compounds at cloned human delta and mu opioid receptors," *J. Pharmacol. Exp. Ther.*, 277(3):1284-1291, 1996.
	C20	Koob *et al.*, "Neural substrates of opiate withdrawal," *TINS*, 15(5):186-191, 1992.

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U.S. Patent Documents	Foreign Patent Documents	Other Art
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Other Art (Including Author, Title, Date Pertinent Pages, Etc.)

Exam. Init.	Ref. Des.	Citation
	C21	Liao *et al.*, "De novo design, synthesis, and biological activities of high-affinity and selective non-peptide agonists of the δ-opioid receptor," *J. Med. Chem.*, 41(24):4767-4776, 1998.
	C22	Loh *et al.*, "Molecular characterization of opioid receptors," *Annu. Rev. Pharmacol. Toxicol.*, 30:123-147, 1990.
	C23	Lutz and Pfister, "Opioid receptors and their pharmacological profiles," *J. Receptor Res.*, 12(3):267-286, 1992.
	C24	Martin, "Pharmacology of opioids," *Pharmacol. Rev.*, 35(4):283-323, 1983.
	C25	Okawa *et al.*, "7-arylindenenaltrexones as selective δ1 opioid receptor antagonists," *J. Med. Chem.*, 41:4177-4180, 1998.
	C26	Olson *et al.*, "Endogenous opiates: 1988," *Peptides*, 10:1253-1280, 1989.
	C27	Pert and Snyder, "Opiate receptor: demonstration in nervous tissue," *Science*, 179(4077):1011-1014, 1973.
	C28	Pfeiffer *et al.*, "Psychotomimesis mediated by $/kappa $ opiate receptors," *Science*, 233(4765):774-776, 1986.
	C29	Plobeck *et al.*, "New diarylmethylpiperazines as potent and selective nonpeptidic δ opioid receptor agonists with increased in vitro metabolic stability," *J. Med. Chem.*, 43(21):3887-3894, 2000.
	C30	Olmsted *et al.*, "A remarkable change of opioid receptor selectivity on the attachment of a peptidomimetic κ address element to the δ antagonist, natrindole: 5'[(N2-alkylamindino) methyl]naltrindole derivatives as a novel class of κ opioid receptor antagonists," *J. Med. Chem.*, 36:179-180, 1993.
	C31	Portoghese *et al.*, "7-arylidenenaltrexones as selective δ1 opioid receptor antagonists," *J. Med. Chem.*, 41:4177-4180, 1998.
	C32	Raynor *et al.*, "Pharmacological characterization of the cloned κ-, δ-, and μ- opioid receptors," *Molecular Pharmacol.*, 45:330-334, 1994.
	C33	Reid *et al.*, "Naltrindole, an opioid delta receptor antagonist, blocks cocaine-induced facilitation of responding for rewarding brain stimulation," *Life Sci.*, 52:PL67-71, 1993.
	C34	Saltzman, In: *Drug Delivery: Engineering Principles for Drug Therapy (Topics in Chemical Engineering)*, Oxford University Press, 2001.

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Other Art (Including Author, Title, Date Pertinent Pages, Etc.)

Exam. Init.	Ref. Des.	Citation
	C35	Schiller *et al.*, "The opioid μ agonist/δ antagonist DIPP-NH2[Ψ] produces a potent analgesic effect, no physical dependence, and less tolerance than morphine in rats," *J. Med. Chem.*, 42(18):3520, 1999.
	C36	Sharp and Yaksh, "Pain killers of the immune system," *Nat. Med.*, 3(8):831-832, 1997.
	C37	Simon, "Opioid receptors and endogenous opioid peptides," *Medicinal Res. Rev.*, 11(4):357-374, 1991.
	C38	Stevens *et al.*, "Potent and selective indolomorphinan antagonists of the kappa-opioid receptor," *J. Med. Chem.*, 43(14):2759-2769, 2000.
	C39	Takemori and Portoghese, "Selective natrexone-derived opioid receptor antagonists," *Annu. Rev. Pharmacol. Toxicol.*, 32:239-269, 1992.
	C40	Wei *et al.*, "N,N-diethyl-4-(phenylpiperidin-4-ylidenemethyl)benzamide: a novel exceptionally selective, potent δ opioid receptor agonist with oral bioavailability and its analogues," *J. Med. Chem.*, 43(21):3895-905, 2000.

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